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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : A61F 5/37 — A1

(11) International Publication Number: **WO 98/31308**

(43) International Publication Date: 23 July 1998 (23.07.98)

(21) International Application Number: PCT/US98/01146

(22) International Filing Date: 21 January 1998 (21.01.98)

(30) Priority Data:
60/035,884 21 January 1997 (21.01.97) US

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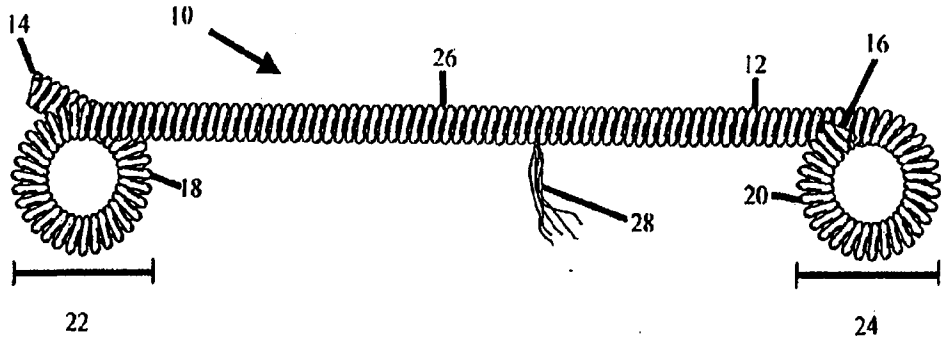
(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published
With international search report.

(54) Title: TRANSCERVICAL CONTRACEPTIVE PLATINUM MICROCOIL



(57) Abstract

The contraceptive microcoil (10) of the present invention provides a contraceptive device suitable for female sterilization. The contraceptive microcoil (10) can be retrievably placed, and thus provides a method for reversible sterilization. The contraceptive device is a contraceptive microcoil (10) comprising a primary coil (12) made of a bio-compatible material, a secondary shape including a distal pigtail, a proximal pigtail, and an intervening segment (26) delimited by the distal pigtail, and the proximal pigtail.

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TRANSCERVICAL CONTRACEPTIVE PLATINUM MICROCOIL

Reference to Related Application

This application claims the benefit of U.S. Provisional Application S.N. 60/035,884, filed January 21, 1997, which is incorporated by reference.

Background of the Invention

There is great demand for an optimal sterilization method in both developed and developing countries (Kessel E, Mumford SD. Potential demand for voluntary sterilization in the 1980s: the compelling need for a non surgical method. Fertil Steril 1982; 37:725-733.). The ideal sterilization procedure should be safe, effective, minimally invasive, non-hormonal, inexpensive, and reversible. Neither traditional laparoscopic surgical approaches nor hysteroscopic techniques fulfill all of these criteria.

There has been an ongoing search for alternative methods of female sterilization that are less invasive, less costly, and more readily reversible than current laparoscopic approaches. Hysteroscopic sterilization techniques are performed with either general or paracervical local anesthesia. The cervic and uterine cavity are sounded and, when necessary, endocervical dilatation is performed. A hysteroscope is then introduced and the uterine cavity is distended with either high molecular weight dextran, dextrose in water, or carbon dioxide gas. Tubal sterilization can then be accomplished via a microcatheter introduced coaxially through the hysteroscope. Uterine perforation is a known complication. Other complications related to distention media include hypercarbia, acidosis, and cardiac arrhythmias due to carbon dioxide intravasation and allergic rections to dextran. In addition, the hysteroscopic sterilization procedure may be unsuccessful in the presence of endometrial bleeding, unremitting tubal spasm, and laterally positioned tubal ostia (Cooper J. Hysteroscopic sterilization. Clin Obstet and Gynecol 1992; 35:282-298.). Such side effects are part of the reason why hysteroscopic methods have not gained widespread clinical acceptance.

It is now possible to achieve transcatheter fluoroscopically guided fallopian tube recanalization using interventional radiologic techniques. (Thurmond A, Rosch J. Nonsurgical fallopian tube recanalization for treatment of infertility. Radiology 1990; 174:571-574). Alternatively, the transcatheter fluoroscopically guided interventional radiologic techniques can be used for fallopian tube occlusion (Maubon A., Selective tubal sterilization in rabbits: experience with a hydrogel combined with a sclerosing agent. Radiology 1994; 193:721-723; Berkey G. et al., Sterilization with Methyl Cyanoacrylate-induced Fallopian Tube Occlusion from a Nonsurgical Transvaginal Approach in Rabbits. JVIR 1995; 6:669-674; Schmitz-Rode, T., et al., Experimental Nonsurgical Female Sterilization: Transcervical Implantation of Microspindles in Fallopian Tubes. JVIR 1994; 5:905-910; Ross, P., et al., Transcatheter tubal sterilization in rabbits: technique and results. Invest Radiol 1994; 29:570-573.) Several recent animal studies have investigated selective tubal catheterization and occlusion as a means of sterilization. Occluding agents that have been tested include hydrogel combined with sclerosing agent (Maubon et al.), methyl cyanoacrylate (Berkey et al.), stainless steel microspindle (Schmitz-Rode, T., et al.), and stainless steel coil (Ross et al.).

Since it is now possible to cannulate the fallopian tubes from a transcervical approach using a fluoroscopically guided microcatheterization technique, there have been several attempts to develop an optimal method of fallopian tubal occlusion for female sterilization. All of the attempts have fallen short of the ideal. Maubon et. al. performed transcatheter tubal sterilization using a hydrogel plug combined with a sclerosing agent. Six of seven rabbits that became pregnant had embryos in the control uterus but not in the uterus on the side of the tubal hydrogel injection. One rabbit had embryos on both the control and hydrogel sides. All of the hydrogel containing tubes showed histologic findings of acute and chronic salpingitis and a foreign body reaction.

Berkey et. al. used intratubal methyl cyanoacrylate in an attempt to achieve permanent sterilization in rabbits. They found a 100 % nonpregnancy rate in

eleven rabbits that underwent six months of mating trials. Histologic examination revealed tubal wall fibrosis with varying degrees of occlusion.

Schmitz-Rode et. al. deployed a tubular metal mesh microspindle in rabbit fallopian tubes for permanent sterilization. Successful contraception was achieved in nine rabbits that had 25 gestations on the nonspindle side and no gestations on the spindle side. One rabbit with a relatively short spindle (9 mm) had pregnancies on both the spindle and nonspindle sides. The spindles were found to be firmly embedded in the tubal wall without evidence of inflammation.

Ross et. al. used a 3.9 cm long, 0.021" diameter stainless steel spring coil placed in a uterotubal location in rabbits in an attempt to develop an efficacious and reversible method of sterilization. The coil was placed with one 3 mm radius loop in the fallopian tube and two similar loops in the uterus. Dislodgement of the coils occurred in 11 of 32 rabbits (34%). When the coil remained in position, it failed to prevent pregnancy in 3 of 19 (16%) rabbits. Ross et. al. speculated that a uterotubal coil might have the high degree of efficacy and the reversibility of the intrauterine device (IUD), but without its associated infectious complications. However, their study showed a contraception failure rate of 44% that was primarily related to coil dislodgement from the fallopian tube.

Contraceptive transcervical fallopian tube occlusion devices are described by international application PCT/US96/07483 ("the '7483 application") published on December 19, 1996 as WO 96/400023. The disclosed devices are formed at least in part from copper or a copper alloy.

U.S. Patent No. 5,601,600 describes endoluminal coil delivery systems, endoluminal coils, and methods for positioning a coil within a body lumen such as the lumen of the fallopian tube. In particular, the patent discloses an improved endoluminal coil comprising a fitting disposed on the coil.

Uterotubal coils have certain similarities to vaso-occulsion devices. Vaso-occlusion devices are surgical implements or implants that are placed within the vasculature of the human body, typically via a catheter, either to block the flow of blood through a vessel making up that portion of the vasculature through the formation of an embolus or to form such an embolus within an aneurysm

stemming from the vessel. One widely used vaso-occlusive device is a helical wire coil having windings which may be dimensioned to engage the walls of the vessels. Other less stiff helically coiled devices have been described, as well as those involving woven braids.

For instance, U.S. Pat. No. 4,994,069, to Ritchart et al., describes a vaso-occlusive coil that assumes a linear helical configuration when stretched and a folded, convoluted configuration when relaxed. The coil is placed in its stretched configuration at the desired site (by its passage through the catheter) and the coil assumes a relaxed configuration—which is better suited to occlude the vessel—once the device is ejected from the catheter and placed. The Ritchart et al. patent discloses a variety of shapes. The secondary shapes of the disclosed coils include "flower" shapes and double vortices. A random shape is described, as well.

Vaso-occlusive coils having attached fibrous elements in a variety of secondary shapes are shown in U.S. Pat. No. 5,304,194, to Chee et al. Chee et al. describes a helically wound device having a secondary shape in which the fibrous elements extend in a sinusoidal fashion down the length of the coil. These coils, as with Ritchart et al., are produced in such a way that they will pass through the lumen of a catheter in a generally straight configuration and, when released from the catheter, form a relaxed or folded shape in the lumen or cavity chosen within the human body. The fibrous elements shown in Chee et al. enhance the ability of the coil to fill space within the vasculature and to facilitate formation of embolus and subsequent allied tissue.

A three dimensional in-filling vaso-occlusive coil is described in U.S. Pat. No. 5,624,461 to Mariant. The device is a complex, helically wound coil comprised of a primary helically wound coil which is then wound into a specific secondary shape. The final shape upon deployment is in the approximate shape of an anatomical cavity. Upon deployment, the device first fills the periphery of the cavity and then continues to in-fill the center. Fibers may be introduced onto the device and affixed to the pre-formed linear member.

Summary of the Invention

We have found that the efficacy of a contraceptive microcoil is greatly enhanced by changes in coil length and secondary shape, and by the addition of fibers. The contraceptive microcoil comprises a resilient primary coil free from any fittings made of a biocompatible material; and a secondary shape including a distal pigtal having at least one turn, a proximal pigtail having at least one turn, and a substantially straight intervening segment delimited by the distal pigtail and the proximal pigtail. The contraceptive utility of a platinum coil embodiment of the present invention placed using an interventional radiological transvaginal approach has been demonstrated.

Brief Description of the Drawings

In the drawings,

Fig. 1 is a drawing of one embodiment of the contraceptive microcoil;

Fig. 2 is a drawing of another embodiment of the contraceptive microcoil;

Fig. 3 is a photograph of an embodiment of the contraceptive microcoil comprising polyester fibers and a 3 mm pigtail at each end;

Fig. 4 is a typical normal left hysterosalpingogram of a rabbit, showing vagina (large straight arrows), uterine horn (small straight arrows), fallopian tube (curved arrows), and free spillage of contrast into the peritoneal cavity (outline arrow);

Fig. 5 is a hysterogram obtained after placement of a contraceptive microcoil in a rabbit, showing the air filled vagina (large straight arrow), uterine horn (small straight arrow), and 7 cm microcoil (curved arrows) positioned in uterine horn and right fallopian tube;

Fig. 6 is a radiograph of the rabbit of Fig. 5, showing the empty uterine horn on the microcoil side (short arrow), the uterotubal junction (long arrow), and eight gestational sacs in the control uterine horn (curved arrows);

Fig. 7 is a photomicrograph of a fallopian tube after microcoil removal, showing dilation of the lumen (L) by the presence of the microcoil, loss of most of the mucosal epithelium (arrow), increased fibrous connective tissue (F) in the

lamina propria and occasional inflammatory cells (hematoxylin and eosin stain, photographed at 50X magnification); and

Fig. 8 is a photomicrograph of a uterine horn after microcoil removal, showing circular defect (D) associated with the presence of the microcoil characterized by a focal loss of adjacent mucosal epithelium, and clusters of sloughed epithelial cells and inflammatory cells present between papillary proliferative structures (arrow) of the endometrial epithelial cells. (hematoxylin and eosin stain, photographed at 30X magnification).

Detailed Description of Preferred Embodiments

The preferred embodiments of the invention are contraceptive microcoils comprising a resilient primary coil having distal and proximal ends. The resilient primary coil is formed into a secondary shape which is assumed when the contraceptive microcoils is in a relaxed state. Fibrous materials may be woven into, wrapped around, or tied to the primary coil or, alternatively, attached to the primary coil using a suitable adhesive.

The contraceptive microcoil is made of a radiopaque, biocompatible material. The biocompatible material is chosen from the group consisting of platinum, gold, iridium, tungsten, stainless steel, nickel, titanium and alloys thereof. Preferred alloys are nickel titanium shape memory alloys (nitinol). Preferably the contraceptive microcoil is made of platinum. Bioactive substances, such as copper and copper alloys, are not suitable for the practice of the present invention.

The resilient primary coil is formed by a wire wound in a helix or by several wires or fibers braided into a hollow tube. Preferably the resilient primary coil is formed from wire ranging from about 0.010 inch (0.254 mm) to about 0.038 inch (0.965 mm) in diameter, more preferably ranging from about 0.010 inch (0.254 mm) to about 0.025 inch (0.635 mm) in diameter. In one preferred embodiment the resilient primary coil is formed from platinum wire 0.018 inch (0.457 mm) in diameter. The primary coil is free from any fittings, such as endcaps or tips, attached to or disposed on the resilient primary coil.

The outer diameter of the primary coil, including any fibers, is chosen to be less than the inner diameter of the delivery catheter. A preferred outer diameter for the primary coil, including fibers, is from about 0.018 inch (0.457 mm) to about 0.032 inch (0.813 mm).

The resilient primary coil is formed into a secondary shape comprising at least one distal pigtail and at least one proximal pigtail. Pigtails are defined herein as loosely cylindrical stacks of secondary coils comprising multiple turns. Such multiple turns of secondary coils are designed to provide solid and robust anchoring of the contraceptive microcoil within the fallopian tube. It should be understood, however, that, due to the interaction of the secondary shape of the contraceptive microcoil and the inner surface of the fallopian tube, the secondary shape in situ may differ from the secondary shape that the contraceptive microcoil would assume in its unrestrained relaxed state.

The proximal pigtail provides a convenient attachment site that can be snared and gently pulled when retrieving the contraceptive microcoil. The tension applied when gently pulling the proximal pigtail of the contraceptive microcoil acts to straighten the contraceptive microcoil, reducing the volume of the secondary shape and thereby facilitating the removal of the contraceptive microcoil from the fallopian tube.

Preferably each of the distal and proximal pigtails comprise loosely cylindrical stacks of from one to ten turns. More preferably, the distal and proximal pigtails comprise stacks of from one to five turns. In one preferred embodiment, the distal and proximal pigtails have different numbers of turns.

The contraceptive microcoil can be temporarily constrained in a straightened configuration and placed into a suitable delivery catheter having distal and proximal openings. The delivery catheter containing the constrained contraceptive microcoil can be situated with the distal opening of the catheter in the lumen or body cavity to be occluded. The contraceptive microcoil is then pushed through the catheter, and, upon ejection from the catheter, assumes its secondary shape in its relaxed state when unconstrained by the delivery catheter.

Referring now to Fig. 1, a first embodiment of the present contraceptive microcoil 10 is formed from a resilient primary coil 12. The resilient primary coil 12 is formed from a biocompatible material chosen from the group consisting of platinum, gold, iridium, tungsten, stainless steel, nickel, titanium and alloys thereof; a preferred biocompatible material is platinum wire. The contraceptive microcoil 10 has a distal end 14 and a proximal end 16. "Proximal" and "distal" are defined herein with respect to the contraceptive microcoil's placement in the fallopian tube, and thus "distal" is defined as "nearer the ovary" and "proximal" is defined as "nearer. the uterus." The resilient primary coil lacks any fittings attached to or disposed on the resilient primary coil. The distal end 14 and the proximal end 16 are free from additional fittings such as endcaps or tips.

During manufacturing, the contraceptive microcoil is formed into a secondary shape that the contraceptive microcoil tends to assume in the relaxed state when freed from stress or constraint. When deployed within the fallopian tube, the contraceptive microcoil assumes its secondary shape, but since the coil is limited by its contacts made with the internal surface of the fallopian tube, the contraceptive microcoil may not completely assume its relaxed state. The structures of the secondary shape such as the distal and proximal pigtails contact, at least in part, the internal surface of the fallopian tube, thereby securing the contraceptive microcoil within the fallopian tube. It should be understood, therefore, that characteristics of the secondary shape, e.g., the diameter of the turns of the distal and proximal pigtails or the number of turns of the when placed in the fallopian tube may vary from the relaxed state depending on the placement of the contraceptive microcoil and the dimensions of the particular fallopian tube.

The structures of the secondary shape of the contraceptive microcoil comprise a distal pigtail comprising at least one turn 18 and a proximal pigtail comprising at least one turn 20. The proximal and distal pigtails each comprise stacks of about one to about ten turns. In one preferred embodiment, the distal and proximal pigtails comprise stacks of about one to about five turns. In another preferred embodiment, the distal and proximal pigtails comprise stacks of about

two to about six turns. In one preferred embodiment, the distal and proximal pigtails have different numbers of turns.

The outer diameter **22** of the turn of the distal pigtail and the outer diameter **24** of the turn of the proximal pigtail in the unconstrained relaxed state range from about 1 mm to about 10 mm, preferably from about 1.5 mm to about 7.5 mm, more preferably from about 1.5 mm to about 5 mm. In one preferred embodiment, the outer diameter **22** of the turn of the distal pigtail and the outer diameter **24** of the turn of the proximal pigtail are both about 3 mm. In other embodiments, the outer diameter **22** of the turn of the distal pigtail may be different from that of the outer diameter **24** of the turn of the proximal pigtail. In one embodiment the outer diameter **22** of the turn of the distal pigtail is smaller than the outer diameter **24** of the turn of the proximal pigtail.

If a pigtail has more than one turn, the outer diameters of the turns within a pigtail can be different. In one embodiment, the outer diameters of the turns may decrease progressively from turn to turn from the end of the primary coil to the nearer end of the intervening segment, approximating a funnel shape. In a preferred embodiment, the outer diameters of the turns with each pigtail are within ±50% of the average outer diameter, preferrably within ± 20% of the average diameter.

The distal end and proximal end may terminate within the boundary of the turn of the respective pigtail, as shown in Fig. 1 for the proximal end **16**. Alternatively, either or both ends may extend beyond the boundary of the turn of the respective pigtail, as shown in Fig. 1 for the distal end **14**.

The intervening segment **26** is delimited by the distal pigtail and the proximal pigtail. The intervening segment **26** is substantially straight in the relaxed state of the contraceptive microcoil, that is, the radius of curvature of intervening segment **26** is greater than the length of intervening segment **26**. The intervening segment **26** is about one cm to about ten cm in length. Preferably the intervening segment is about three to about seven cm in length.

Fibers **28** are optionally disposed on the resilient primary coil along the length of the resilient primary coil. For clarity only a few fibers are illustrated at

one position in Fig. 1. However, it should be understood that the fibers **28** are present over a substantial portion of the length of the resilient primary coil. In different embodiments fibers **28** are restricted to the intervening segment or to the distal and proximal pigtails. In a preferred embodiment, the fibers **28** are distributed along the entire length of the resilient primary coil; see Fig. 3.

The fibers **28** may be arranged as individual fibers or as clumps of fibers. The fibers **28** are disposed on the primary coil using any of a number of suitable means. The fibers **28** may be wrapped around or intertwined with the wire that forms the primary coil **12**. Alternatively, the fibers may be bonded to the primary coil **12** using an appropriate adhesive. Suitable fibers are made from biocompatible polymeric materials, such as polyesters. Preferred polyester fibers include polyethylene terephthalate, which is commercially available as Dacron™ (Du Pont).

In the embodiment illustrated in Fig. 1, the distal end **14** and the at least one turn **18** of the distal pigtail extend below the plane of the intervening segment **26** while the proximal end **16** and the at least one turn **20** of the proximal pigtail extend above the plane of the intervening segment **26**. Alternatively, in one preferred embodiment, the distal end **14** and the at least one turn **18** of the distal pigtail extend on the same side of the plane of the intervening segment **26** as the proximal end **16** and the at least one turn **20** of the proximal pigtail.

In the embodiment illustrated in Fig.1, the longitudinal axis of the distal pigtail (defined as a line passing through the center of the at least one turn **18** of the distal pigtail and perpendicular to the plane of the turn) and the corresponding longitudinal axis of the proximal pigtail are approximately perpendicular to the plane of the intervening segment **26**. Alternatively, in another embodiment, the longitudinal axes of both the proximal pigtail and the distal pigtail are roughly parallel to the plane of the intervening segment in the relaxed state. In one preferred embodiment, the longitudinal axes of both the proximal pigtail and the distal pigtail are roughly perpendicular to the plane of the intervening segment and both the proximal pigtail and the distal pigtail extend on the same side of the plane of the intervening segment in the relaxed state.

Referring now to Fig. 2, a second embodiment of the present contraceptive microcoil **30** is formed from a resilient primary coil **32**. The resilient primary coil **32** is formed from a biocompatible material; a preferred biocompatible material is platinum wire. The contraceptive microcoil **30** has a distal end **34** and a proximal end **36**. The distal end **34** and the proximal end **36** are free from additional fittings such as endcaps or tips. The structures of the secondary shape of the contraceptive microcoil comprise a distal pigtail comprising at least one turn **38** and an opposing proximal pigtail comprising at least one turn **40**. The proximal and distal pigtails each comprise stacks of about one to about ten turns. In one preferred embodiment, the distal and proximal pigtails comprise stacks of about one to about five turns. In another preferred embodiment, the distal and proximal pigtails comprise stacks of about two to about six turns. In one preferred embodiment, the distal and proximal pigtails have different numbers of turns.

The outer diameter **42** of the turn of the distal pigtail and the outer diameter **44** of the turn of the proximal pigtail in the unconstrained relaxed state ranges from about 1 mm to about 10 mm, preferably from about 1.5 mm to about 7.5 mm, more preferably from about 1.5 mm to about 5 mm. In one preferred embodiment, the outer diameter **42** of the turn of the distal pigtail and the outer diameter **44** of the turn of the proximal pigtail are both about 3 mm. In other embodiments, the outer diameter **42** of the turn of the distal pigtail may be different from that of the outer diameter **44** of the turn of the proximal pigtail. In one embodiment the outer diameter **42** of the turn of the distal pigtail is smaller than the outer diameter **44** of the turn of the proximal pigtail.

The distal end and proximal end may terminate within the boundary of the turn of the respective pigtail, as shown in Fig. 2 for both the distal end **34** and the proximal end **36**. Alternatively, the either or both ends may extend beyond the boundary of the turn of the respective pigtail.

The intervening segment **46** is delimited by the distal pigtail and the proximal pigtail. The intervening segment **46** is substantially straight in the relaxed state of the contraceptive microcoil, that is, the radius of curvature of intervening segment **46** is greater than the length of intervening segment **46**. The

intervening segment **46** is about one cm to about ten cm in length. Preferably the intervening segment is about three to about seven cm in length.

In the embodiment illustrated in Fig. 2, the distal end **34** and the at least one turn **38** of the distal pigtail extend below the plane of the intervening segment **46** while the proximal end **36** and the at least one turn **40** of the proximal pigtail extend above the plane of the intervening segment **46**. Viewed perpendicular to the plane of the intervening segment **46**, the distal pigtail and the proximal pigtail are on opposite sides of the intervening segment **46**; thereby increasing the volume occupied by the secondary shape of the contraceptive microcoil in its relaxed state. Alternatively, in one preferred embodiment, the distal end **34** and the at least one turn **38** of the distal pigtail extend on the same side of the plane of the intervening segment **46** as the proximal end **36** and the at least one turn **40** of the proximal pigtail.

In one preferred embodiment, fibers are disposed along the primary coil **32**. The fibers may be arranged as individual fibers or as clumps of fibers. The fibers may be intertwined with the wire that forms the primary coil **32**. Alternatively, the fibers may be bonded to the primary coil **32** using an appropriate adhesive. Suitable fibers are made from biocompatible polymeric materials, such as polyesters. Preferred polyester fibers include polyethylene terephthalate, which is commercially available as Dacron™ (Du Pont).

Example 1

The contraceptive microcoil was constructed from 0.018 inch (0.46 mm) diameter platinum wire that was formed into a primary coil and having a secondary configuration of a distal pigtail about 0.12 inch (3 mm) in diameter comprising about two turns, a proximal pigtail about 0.12 inch (3 mm) in diameter comprising about four turns, and an intervening segment separating the distal pigtail from the proximal pigtail (Fig. 1, Fig. 3). The length of the intervening segment was either about two inches (5 cm), about 2.4 inches (6 cm), or about 2.75 inches (7 cm). Polyester fibers (polyethylene terephthalate, Dacron™, Du Pont) were deposed along the length of the microcoil.

Rabbits were housed and maintained in compliance with the "Principles of Laboratory Animal Care" (formulated by the National Society for Medical Research) and the "Guide for the Care and Use of Laboratory Animals" (NIH Publication no. 80-23, revised 1985). Rabbits were chosen for the initial tests of the contraceptive microcoil because they have two separate uteri, each with its own fallopian tube. The method and device of the present invention may be used, with modifications apparent to one skilled in the art, to treat females of other mammalian species, including humans

A contraceptive microcoil was placed in the fallopian tube and uterus of one side in each animal. The contralateral tube and uterus served as an internal control. Ten virgin female New Zealand White rabbits were fitted with contraceptive microcoils; two male New Zealand White rabbits were used for breeding purposes. The body weight of the animals was 4.0 - 5.0 kg.

The animals were anesthetized by intramuscular (IM) injection with a combination of ketamine (30 mg/kg IM), xylazine (5 mg/kg IM), and acepromazine (1 mg/kg IM). Additional doses of these drugs were administered intravenously as needed during the surgical procedure to maintain anesthesia at a level necessary for surgery. The animals were placed supine on the fluoroscopy table and the vaginal region was prepped with povidone iodine solution. Fallopian tube catheterization was then performed using a technique similar to that of Thurmond et. al. (Thurmond, A., et al., Transvaginal fallopian tube catheterization in an animal model. Invest Radiol 1988; 23:818-821). Specifically, a double-port 18 French (F) Foley catheter with a 30 cc balloon (Bard, Covington, Ga), stiffened by an 8 F Lumax guiding catheter (Cook, Inc., Bloomington, IN) was used to catheterize the vagina (base catheter). In three early cases, a 9 F Teflon transjugular catheter (Cook, Inc., Bloomington, IN) was used as an alternative to the Foley/Lumax combination.

When using the Foley/Lumax combination, the distal tip of the Foley catheter was cut off, and the catheter was inserted into the vagina with the aid of a water soluble lubricant (K-Y Jelly, Johnson and Johnson, Skillman, NJ). The balloon was then inflated with 20-30 cc of air. Air was then injected through the

Foley side port to distend the vaginal vault, thus allowing visualization of the two cervices. A 5 F MPA Torcon catheter (Cook, Inc., Bloomington, IN) was introduced through the base catheter into one of the two cervices with the aid of a .035" Glidewire (Terumo, Piscataway, NJ, distributed by Medi-tech/Boston Scientific, Watertown, MA). The uterine horn was opacified with iodinated contrast material (Hypaque 60, Nycomed, Inc., New York, NY) and air. The 5 F catheter was advanced to the cornual region over a .035" Bentson guide wire (Cook, Inc, Bloomington, IN). In some cases, the 5 F catheter was successfully advanced into the interstitial segment of the fallopian tube in this manner. In other cases, a 3 F nylon catheter (Cook, Inc, Bloomington, IN) or a Tracker-18 catheter (Target Therapeutics, Inc., Fremont, CA) was introduced coaxially to gain access to the fallopian tube with the aid of a .018" Torq-Flex (Cook, Inc., Bloomington, IN) guidewire or a .018" Glidewire. A small amount of contrast was then injected, and fallopian tube patency was confirmed fluoroscopically in all cases. The coil was always deployed through a 3 F nylon catheter because it was too large to pass through the lumen of a Tracker-18 catheter. The coil was pushed through the 3 F nylon catheter with the .018" Torq-Flex guidewire and deposited in a position spanning tubal isthmus, interstitial segment, cornual region, and part of uterine horn. The choice of coil length was based on how far the 3 F catheter could be advanced into the fallopian tube. The intent was to deposit the coil, such that two-thirds of its length would be in the fallopian tube and one third would be in the uterus. Positioning the coil in this manner would allow testing its contraceptive effectiveness, and, at the same time, leave the door open to snare retrieval of the coil and reversal of the contraceptive effect. Final coil position was documented with a post-procedure hysterosalpingogram.

Rabbits were bred after a rest period of 13-15 days. Pregnancy was detected by palpation 10-14 days following the breeding session. The rabbits were then sacrificed before the expected delivery date. Abdomen and pelvis of all animals were grossly inspected for location of embryos, and presence or absence of abscesses, adhesions, ectopic pregnancies, or other abnormalities. The uteri and attached fallopian tubes and ovaries were removed, and a specimen radiograph

obtained to re-evaluate coil position. The specimen was placed in formalin. In order to obtain tissue sections, it was necessary to remove the coil. This was accomplished after fixation by manually pulling on its uterine end. Full thickness transverse sections were made of fallopian tube and uterine tissue surrounding the: (1) microcoil pigtail within the fallopian tube, (2) microcoil straight segment within the fallopian tube, (3) microcoil straight segment at the uterotubal junction, (4) microcoil pigtail within the uterine horn, (5) uterus below coil, (6) fallopian tube above coil, (7) contralateral fallopian tube, (8) and contralateral uterine horn. The specimens were processed for histologic evaluation in accordance with standard procedures, stained with hematoxylin and eosin, and evaluated microscopically by a veterinary pathologist .

A contraceptive microcoil was inserted into one fallopian tube and uterine horn in each of ten rabbits. The coil was advanced 1.5 cm - 6 cm (mean 3.25 cm) into the fallopian tube. There was a coil length of 1.5 - 5.5 cm (mean 3.05 cm) extending into the uterine horn. In one early animal, the coil was inadvertently placed entirely into the fallopian tube (coil length 6 cm). In all other animals, the coil was uterotubal in location. All fallopian tubes were demonstrated to be patent by selective salpingography prior to coil placement.

Eight rabbits became pregnant after one breeding session and one became pregnant after a second session. One rabbit failed to become pregnant despite four breeding attempts. Eight rabbits were killed 26-35 days (conceived with one breeding session) after coil insertion. The other two rabbits were killed at 50 days (conceived with two breeding sessions) and 75 days (did not conceive despite four breeding attempts) post coil insertion.

In nine rabbits, there were no embryos on the microcoil side and 2-8 (mean 5) embryos on the control side. This group included the rabbit with the coil entirely within the fallopian tube. In one rabbit, there were no embryos on either side. Gross inspection and specimen radiography revealed no significant coil migration or dislodgement in any of the animals.

Gross inspection at autopsy revealed no evidence of ectopic pregnancy, abscess, adhesions, uterotubal perforation or other significant abnormality in any

of the rabbits. Histologic evaluation of fallopian tubes and uteri was performed on all ten rabbits. Lesions were identified within the tissues that were in contact with each microcoil. No differences were observed between the two rabbits exposed to the coils for 50 and 75 days compared to the remaining eight rabbits exposed for 26-35 days.

The fallopian tubes exposed to the coils contained focal circular compressed areas of the mucosa, lamina propria, and occasionally the muscular wall that correlated with the size and shape of the pigtail of the coil. There was atrophy and loss of mucosal epithelial cells associated with the defects. There were occcasional heterophils, mild fibrovascular tissue proliferation within the adjacent lamina propria, and occasional mild proliferative changes within regenerating mucosal epithelium, including foci of squamous metaplasia. There were also occasional foci of coil associated refractile particles of polyester fibers that were partially surrounded by macrophages and multinucleated giant cells.

The uteri exposed to the contraceptive microcoils also contained focal circular compressed disrupted areas of the mucosa and lamina propria surrounding the pigtail of the coil, as well as epithelial cell degeneration and necrosis with mild numbers of heterophils in the adjacent lamina propria. Some of the affected areas contained increased fibrous connective tissue and increased numbers of small caliber blood vessels within the lamina propria. There were sloughed epithelial cells and heterophils with the lumen. Mild focal proliferative or regenerative changes were seen within mucosal epithelium that contained enlarged nuclei with prominent nucleoli and occasional mitotic figures. There were also occasional mitotic figures within mesenchymal cells of the lamina propria. Occasional multinucleated epithelial cells and foci of squamous metaplasia were seen within the mucosa. Small clusters of placental cytotrophoblastic and syncytotrophoblastic cells were embedded within the uterine mucosa exposed to the coil in three rabbits.

Sections from the nine gravid uteri, one non-gravid uterus, and the ten fallopian tubes not exposed to the contraceptive microcoils were normal. Sections from uteri caudal to the level of the coil were normal in seven rabbits and showed

mild mucosal epithelial proliferative changes in three rabbits. Sections from fallopian tubes cephalad to the level of the microcoil were normal in all cases.

The coil used in this study prevented pregnancy and remained in position in all animals. The relatively increased effectiveness may due to greater length of coil in the fallopian tube, different coil configuration, polyester fibers, or a combination of these factors. The contraceptive action of the coil may also be due, at least in part, to a local IUD-like effect upon the uterine endometrium.

Histopathologically, we found mild coil-associated necrosis, inflammation, and fibrosis in the fallopian tubes and uteri. These tissue changes occurred prior to fixation and are therefore related to the presence of the coil rather than representing artifacts associated with its removal. It is possible that some of the loss of mucosal epithelium may have been partially related to coil removal.

While not being restricted to one hypothesis, it is believed that the contraceptive effect of this type of device may be related to interference with normal movement of the embryo through the tube and into the uterus (Ross et al.; Schmitz-Rode et al., and Brundin). However, the presence of placental tissue in the wall of three of the coil-exposed uteri suggests that a limited amount of embryo implantation occasionally did occur. This indicates that, in at least some instances, failed conception was due to interference with continued implantation and early development of fertilized ova.

Failed conception has been associated with chronic inflammation of the uterus and fallopian tubes of multiple infectious causes. The localized inflammation caused by the implanted coils appeared due to the physical disruption and necrosis of epithelial and mesenchymal cells surrounding the coils. Necrotic cells release cytokines and other factors which attract segmented leukocytes, favor fibrovascular tissue production, and probably disrupt the delicate environment required to sustain pregnancy. Although the lesions were microscopic and localized to the vicinity of the coil, pregnancy either did not occur or failed to progress anywhere within the uterine horn. The lesions associated with the coil were mild focal microscopic changes that do not appear severe enough to preclude its use as a contraceptive device, at least during the time period of this study.

Refinement of the deployment technique can produce more precise positioning of the coil. The variability in coil position between animals in this study was primarily due to uterotubal spasm and resultant inability to determine the exact location of the uterotubal junction at the time of coil deployment. Based on the findings of this study, a contraceptive microcoil, preferably placed in an uterotubal position, can be a safe, effective, and minimally invasive means of female sterilization.

Example 2

A contraceptive microcoil is retrievably placed in each of the fallopian tubes of a human female using a modification of the basic technique outlined in detail in Example 1. The sterilization provided by the contraceptive microcoil is reversed by removal of each contraceptive microcoil by snaring the proximal pigtail of the microcoil and pulling the contraceptive microcoil gently from the fallopian tube.

The contraceptive microcoil of the present invention is deployed in the human female with tubal catheterization techniques that are already in use for fallopian tube recanalization. The procedure is less invasive and less costly than laparoscopic and hysteroscopic techniques because of simpler, less costly instrumentation, transvaginal rather than transperitoneal approach, and lack of need for anesthesiology support. The design of the contraceptive microcoil also would minimize the incidence of associated uterine and tubal infection compared to the intrauterine device (IUD), since the contraceptive microcoil does not have a string extending into the vagina. The contraceptive microcoil of the present invention can also be retrieved with a snare from a transcervical approach.

The patient is consented for the tubal sterilization procedure and is then placed in the dorsal lithotomy position on a fluoroscopic table. The skin of the perineum is sterily prepared and draped using iodine-povidone solution (or Hibiclens™ if iodine allergic). A sterile speculum is inserted and the internal vaginal vault sterily prepared. The patient is sedated to a level of light conscious sedation using midazolam and fentanyl administered intravenously.

The external cervical os is cannulated with a cervical canulation device designed for this purpose. The inner lumen of the cervical cannulation device is large enough to accommodate coaxial introduction of a 5F to 7F 60 degree angled cather made of Teflon™ or other low friction material into the uterine cavity. This angled catheter has an inner lumen of about .038 inch (0.965 mm). The 60 degree angled design of angled catheter permits insertion of the tip of this catheter into the fallopian tube ostium at the uterotubal junction. Some of the time this can be done using the angled catheter only and some of the time this maneuver requires the use of guidewires.

Once the angled catheter is engaged into the fallopian tube ostium, a small amount of x-ray dye is injected into the tube to outline its contour and measure its length (this study is called a direct salpingogram). Based on the direct salpingogram, a contraceptive microcoil having the most appropriate length and pigtail configuration are chosen from among several available.

Next, a small flexible catheter about 2.5F to 3.0F in size (e.g 3F polyethylene catheter by Cook, Inc., Bloomington, IN or Tracker-18, Target Therapeutics, Tustin, CA) is passed coaxially through the angled catheter over a 0.10 inch (.254 mm) to .018 inch (.457 mm) highly torqueable and hydrophilic guidewire until the tip of the small flexible catheter lies in the distal isthmic or proximal ampullary portion of the fallopian tube.

The sterilization coil is then loaded into the hub of the small flexible catheter, and advanced using a coil pusher device, and deployed under fluoroscopic control into the fallopian tube so that the distal pigtail of the sterilization coil lies in the mid-ampullary portion of the fallopian tube. The intervening segment of the contraceptive microcoil then occupies the isthmic and interstitial portions of the fallopian tube, and the proximal pigtail reforms into its coiled configuration of the relaxed state in the uterine horn near the uterotubal junction. A similar procedure is performed to the contralateral fallopian tube. At completion hysterosalpingography is performed to assess the adequacy of coil deployment.

Microcoil retrieval is performed to reverse sterilization when appropriate. The procedure involves consent of the patient and placement on a fluoroscopy table in the dorsal lithotomy position. Cannulation of the cervix occurs as outlined above using the same instrumentation. The uterine end of the retrievably placed contraceptive microcoil is captured using a retrieval snare device (Amplatz Gooseneck Snare, Microvena, Vadnais Heights, MN), which is inserted coaxially through the cervical cannulation device device in place of angled catheter described above. The inner component of the Amplatz Gooseneck Snare is a double nitinol wire with a snare loop at the end. When deployed beyond its guiding catheter component, the Gooseneck Snare opens into a circular "lasso" configuration. The snare loop is then placed around the uterine end of the microcoil and the double wire component withdrawn into the guiding catheter to close the snare tightly around the uterine end of the microcoil. Once so engaged, the microcoil is withdrawn from the fallopian tube with gentle traction. The Amplatz Gooseneck Snare and the microcoil are removed from the uterus, cervix, and vagina, leaving the cervical cannulation device still in place. The procedure is repeated to remove the microcoil in the contralateral fallopian tube. A completion hysterosalpingogram is then performed to test for fallopian tubal patency and to confirm that the entire microcoil has been removed.

The foregoing is intended to be illustrative of the present invention, but not limiting. Numerous variations and modifications of the present invention may be effected without departing from the true spirit and scope of the invention.

We claim:

1. A contraceptive microcoil comprising

a resilient primary coil made of a biocompatible material and free from fittings; and having a secondary shape including a distal pigtail having at least one turn, a proximal pigtail having at least one turn and a substantially straight intervening segment delimited by the distal pigtail and the proximal pigtail.

2. The contraceptive microcoil of claim 1 wherein the biocompatible material is chosen from the group consisting of platinum, gold, iridium, tungsten, stainless steel, nickel, titanium and alloys thereof.

3. The contraceptive microcoil of claim 1 wherein the distal pigtail has about one to about ten turns.

4. The contraceptive microcoil of claim 1 wherein the proximal pigtail has about one to about ten turns.

5. The contraceptive microcoil of claim 1 wherein the distal pigtail has about one to about five turns.

6. The contraceptive microcoil of claim 1 wherein the proximal pigtail has about one to about five turns.

7. The contraceptive microcoil of claim 1 wherein the distal pigtail has about two to about six turns.

8. The contraceptive microcoil of claim 1 wherein the proximal pigtail has about two to about six turns.

9. The contraceptive microcoil of claim 1 wherein the intervening segment is about one cm to about ten cm long.

10. The contraceptive microcoil of claim 1 wherein the intervening segment is about 3 cm to about 7 cm long.

11. The contraceptive microcoil of claim 3 wherein the intervening segment is about 3 cm to about 7 cm long.

12. The contraceptive microcoil of claim 1 comprising in addition polyester fibers disposed along the length of the primary coil.

13. The contraceptive microcoil of claim 12 wherein the polyester fibers are polyethylene terephthalate fibers.

14. A method of sterilization of a female mammal comprising the step of placing a portion of a contraceptive microcoil having a distal pigtail, a proximal pigtail and an intervening segment within each fallopian tube.

15. The method of claim 14 wherein the distal pigtail and a part of the intervening segment of the contraceptive microcoil are placed within each fallopian tube.

16. The method of claim 14 wherein the proximal pigtail and a part of the intervening segment of the contraceptive microcoil are placed within the uterus.

17. A method of sterilization of a human female comprising the step of retrievably placing a portion of a contraceptive microcoil having a distal pigtail, a proximal pigtail and an intervening segment within each fallopian tube.

18. The method of claim 14 wherein the distal pigtail and a part of the intervening segment of the contraceptive microcoil are placed within each fallopian tube.

19. The method of claim 17 wherein the proximal pigtail and a part of the intervening segment of the contraceptive microcoil are placed within the uterus.

20. The method of claim 17 comprising in addition the steps of retrieving the contraceptive microcoil and removing the contraceptive microcoil from the fallopian tube.

21. A contraceptive microcoil suitable for the sterilization of a human female comprising:

a primary coil made of a biocompatible material;

polyester fibers disposed along the length of the primary coil; and

a secondary shape including a distal pigtail having at least one turn, a proximal pigtail having at least one turn and a substantially straight intervening segment delimited by the distal pigtail and the proximal pigtail.

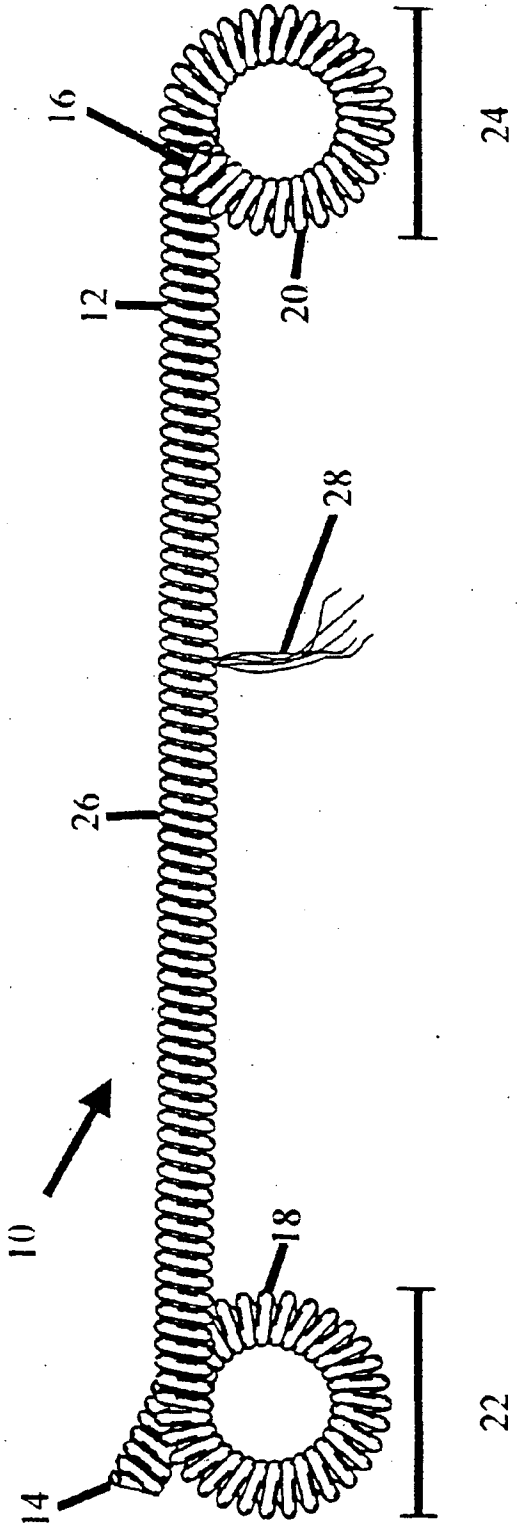

FIG. 1

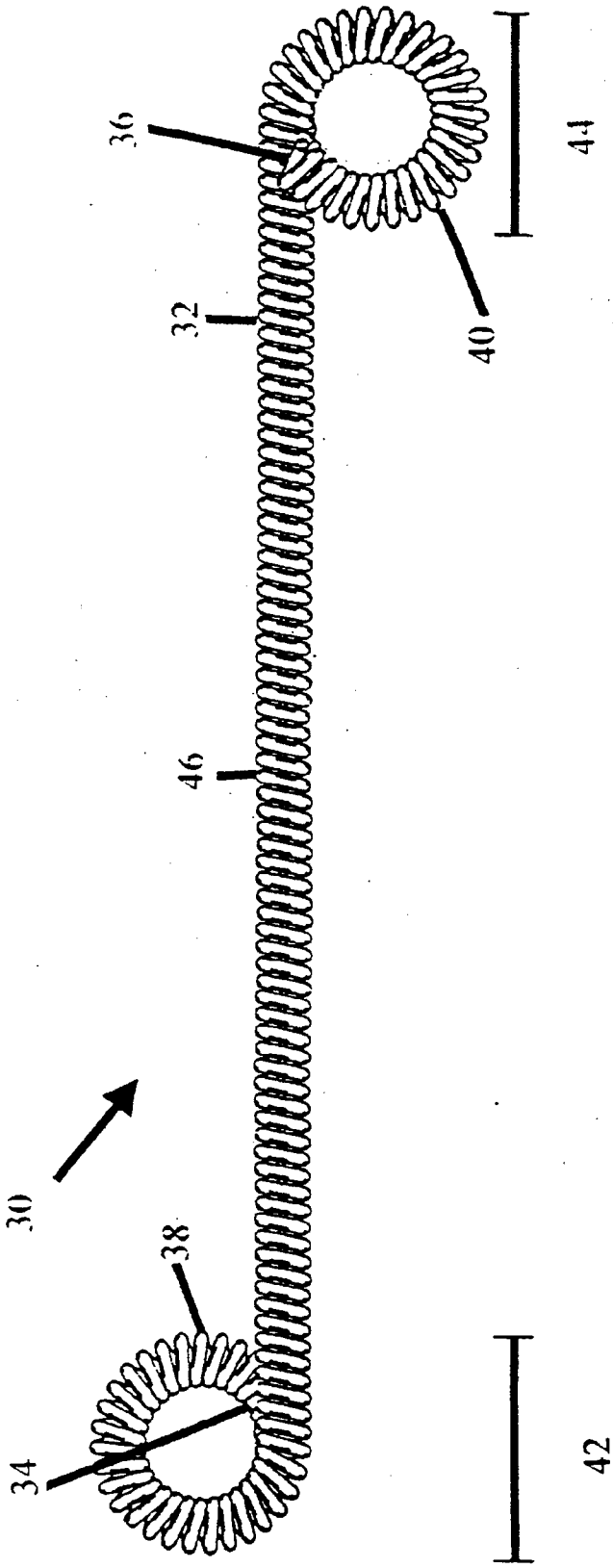

FIG. 2

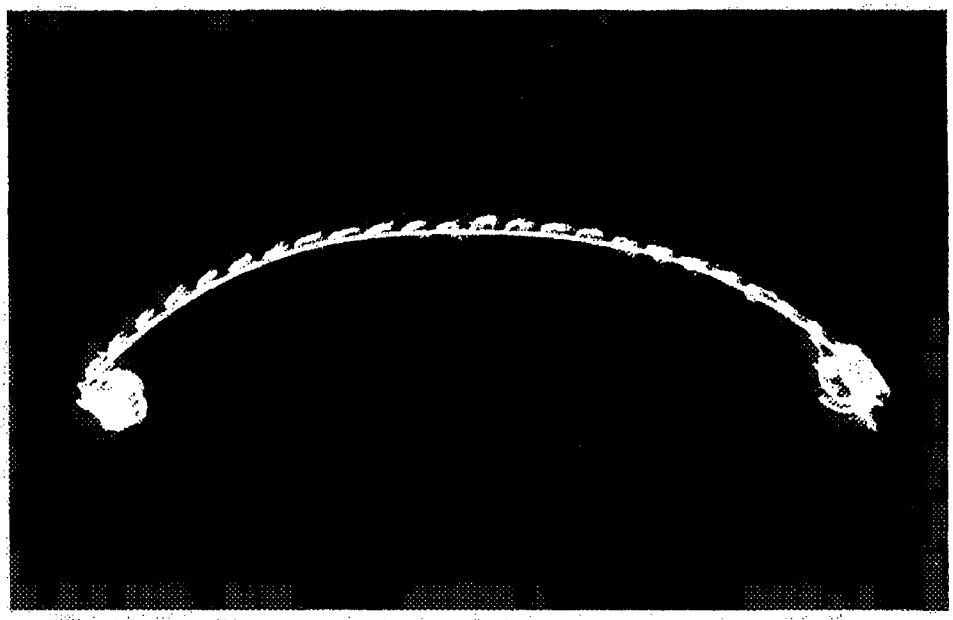

FIG.3

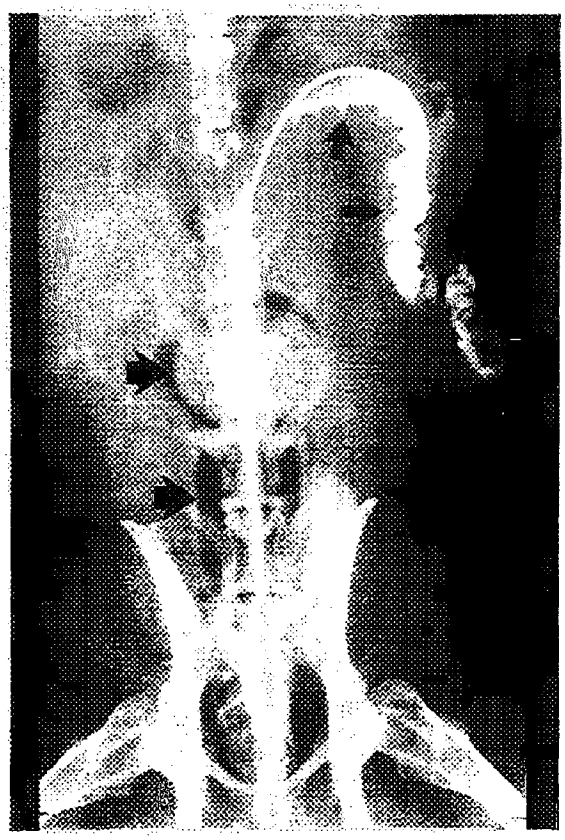

FIG.4

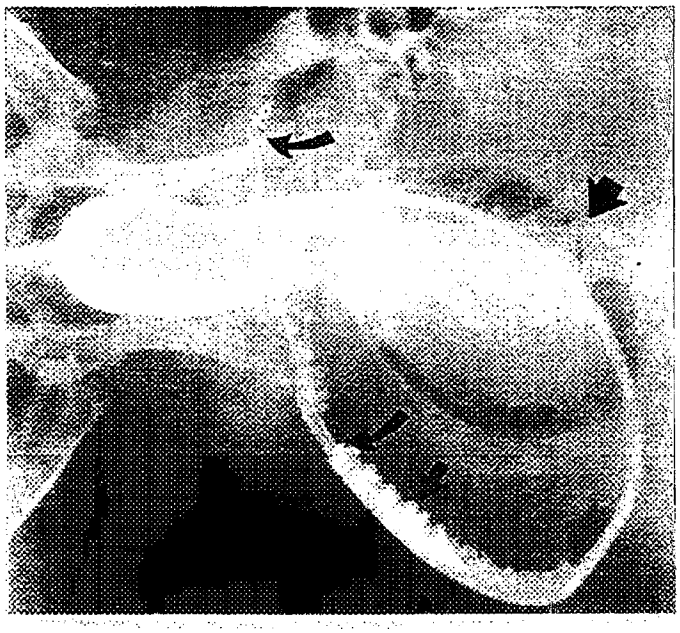

FIG.5

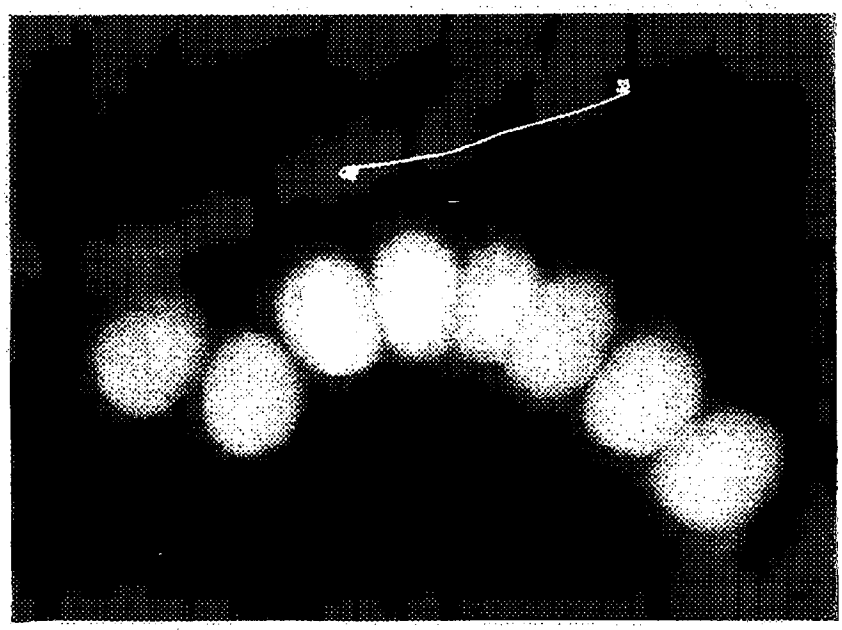

FIG.6

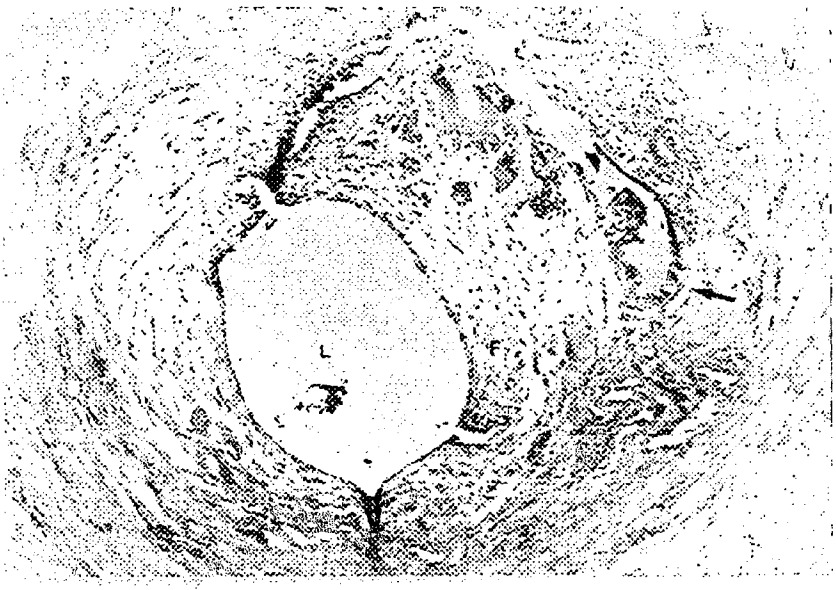

FIG.7

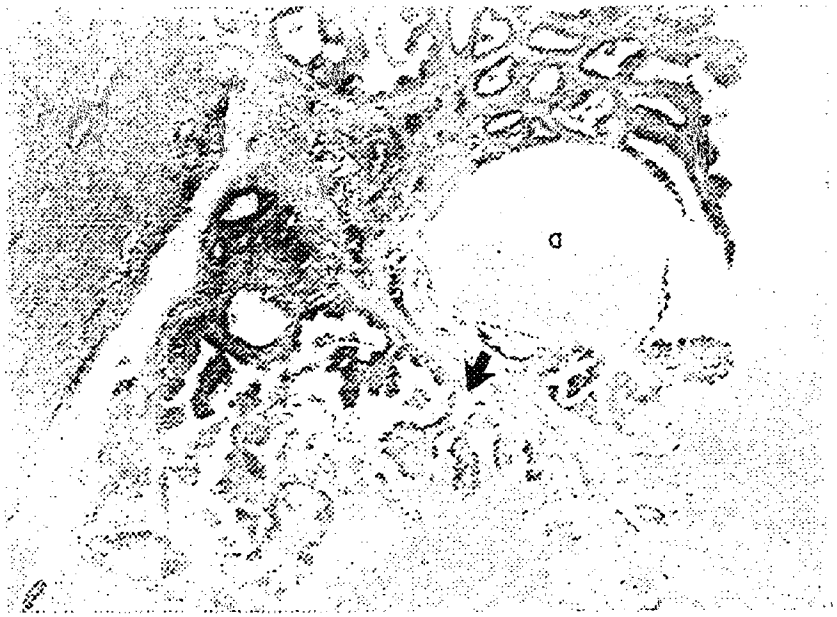

FIG.8

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/01146

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61F 5/37
US CL :128/841

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 128/830-841

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 3,490,456 A (KORTUM) 20 January 1970, entire document.	1, 14, 16, 17, 19
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Y		2-11, 14-20
Y	US 3,858,571 A (RUDOLPH) 07 January 1975, entire document.	2
Y	US 4,595,000 A (HAMOU) 17 June 1986, entire document.	15, 18, 20

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search	Date of mailing of the international search report
13 MARCH 1998	21 APR 1998
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer MICHAEL A. BROWN Telephone No. (703) 308-2682

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